UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF WISCONSIN

PROMEGA CORPORATION,

Plaintiff,

MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN E.V.,

Case No.: 10-CV-281

Involuntary Plaintiff,

v.

LIFE TECHNOLOGIES CORPORATION, INVITROGEN IP HOLDINGS, INC., and APPLIED BIOSYSTEMS, INC.,

Defendants.

PROMEGA CORPORATION'S OPENING CLAIMS CONSTRUCTION BRIEF

Plaintiff Promega believes the claims of the asserted patents[1] are clear and do not need further claim construction by this Court. Defendants, however, have proposed constructions for some claim terms in a chart (attached as Exhibit A hereto) associated with a letter dated February 28, 2011. Plaintiff asks that Defendants' proposed constructions be rejected.

[1] U.S. Patent Nos. 5,843,660 ('660); 6,221,598 ('598); 6,479,235 ('235); and 7,008,771 ('771) (collectively "the Promega Patents") and RE37,984 (the "Tautz patent").

The Defendants' proposed constructions suffer from a host of problems.[2] Generally the Defendants attempt to import limitations that do not appear in the claims themselves, and in the process repeatedly fail to differentiate dependent and independent claims. Their proposed claim construction for "a set of . . . loci" directly conflicts with this Court's claim construction in an earlier case. (*Promega Corp. v. Applera Corp.*, 3:01-CV-244-bbc (W.D. Wis. June 10, 2002) (Order). Perhaps most importantly, the Defendants' proposed constructions, nearly without exception, do not actually offer technical definitions for claim terms; instead, the Defendants state the claim term, add other terms, and then provide an interpretation. The actual meanings of the technical words of the claims appear not to be in dispute.

[2] Defendants have not provided Promega an identification of the specific patents (let alone the specific claims) for which their construction allegedly applies. It appears that Defendants are primarily construing terms in the Promega Patents—with only one term ("gel") possibly applicable to the Tautz Patent.

I. TECHNOLOGY BACKGROUND

The preamble to many of the claims of the Promega Patents[3] describes the inventions as "[a] ***method*** of simultaneously determining the ***alleles*** present in a set of ***short tandem repeat loci*** from one or more DNA samples, comprising . . ." (Preamble to Claim 12, '598 Patent at Col. 39, lines 31-32) (emphasis added). In order to understand such language, the nature of the particular genetic markers specified in Promega's patents, and how they are analyzed according to the methods and kits claimed in the patents, an overview of the makeup of the human genome is helpful.

Briefly, the human genome is comprised of the DNA present in the 23 pairs of chromosomes existing in the nucleus of human cells. (Dimond Declaration, ¶ 4).This genomic DNA is made of two complementary "strands" or "sequences" of "nucleotides" or "bases." The nucleotides in DNA are only four in number and are paired in a defined manner. The four nucleotides are adenine (A), thymine (T), guanine (G) and cytosine (C).[4] An (A) is complementary to, and pairs only with (T); a (C) is complementary to, and pairs only with a (G). (*Id*.) With this basic understanding, the principles for determining genetic identity can be discussed.

[3] The Promega Patents are all in a lineage that dates back to an original (parent) U.S. Patent Application Serial No. 08/316,544, filed September 30, 1994. The '598 Patent issued from a continuation application off of this original filing (and contains no new matter). The '660 Patent is a continuation-in-part off of this original filing (and contains new matter). The '235 Patent is a continuation-in-part off of the '660 (and thus contains material in addition to the new matter of the '660 Patent). Finally, the '771 Patent is a divisional off of the '235 Patent (and thus has a specification that is identical to the '235 Patent).

[4] As noted in the '598 Patent (Col. 5, lines 23-25), "the nucleotide bases are designated as adenine (A); thymine (T); guanine (G); and cytosine (C)."

A. The Use of Polymorphic Loci For Determining Genetic Identity

The basic principle underlying genetic identity testing is that the combination of genetic information at multiple locations in genomic DNA are unique to each individual. (Dimond Declaration, ¶ 5). As a result, in order to use DNA to identify an individual, one can target and identify certain locations or "loci" on the chromosomes,[5] which are polymorphic within a population, *i.e.*, loci which vary from individual to individual within the population.[6] These loci are useful as identifiers only when they exhibit a high degree of variation within the population, since if they were largely the same from individual to individual within the population, their ability to distinguish any one individual from another would be minimal. (Dimond Declaration, ¶ 5). The more a specified locus varies within a population, *i.e.*, the more it varies from individual to individual, the more "polymorphic" the locus is said to be. No one locus alone, however, will positively identify an individual to a statistically significant degree, since no one locus is unique to each individual within any given population. (Dimond Declaration, ¶ 6). Consequently, for purposes of forensic and paternity determinations, the identification of multiple polymorphic loci is necessary. Indeed, the more polymorphic the loci used in the identification process, the more accurate the identification becomes because the statistical probability of a match between the DNA sample and the individual in question increases exponentially as additional matching loci are identified. (Dimond Declaration, ¶ 6). The goal is to use enough loci with sufficient polymorphic characteristics such that the identification is so statistically significant that the result

[5] As noted in the '598 Patent (Col. 5, lines 30-31) a "locus" is a "specific position on a chromosome."

[6] As noted in the '598 Patent (Col. 5, lines 26-28) "DNA polymorphism" is "the condition in which two or more different nucleotide sequences coexist in the same interbreeding population in a DNA sequence."

cannot be reasonably disputed, *i.e.*, the individual is identified beyond any reasonable doubt.[7] For example, using Promega's genetic identity products, one can identify an individual's DNA with a power of discrimination exceeding 1 in 100,000,000,000. (Dimond Declaration, ¶ 7).

The polymorphic loci that are the subject of the Tautz Patent and Promega Patents are known as "short tandem repeats" or "STRs." STRs are loci found within genomic DNA that have a number of short repetitive nucleotide sequences. Different authors have slightly different definitions with regard to the repeat length that is considered an STR. (Dimond Declaration, ¶ 8). As noted in the Promega Patents: "STR loci consist of short, repetitive sequence elements of 3 to 7 base pairs in length." ('598 Patent at Col. 1, lines 32-33). However, the Tautz Patent refers to these same repeat types as having repeat lengths from 3 to 10 nucleotides. Any differences in these definitions, however, do not appear to have an impact on the issues in this case. (Dimond Declaration, ¶ 8).

The DNA sequences at a particular STR locus within a given population will exhibit a variable number of these repeat sequences. For some individuals within a given population the sequence will repeat 7 times, for others 8 times, for others 4 and so on. It is this variation in the number of repeats at a particular locus that is responsible for the polymorphisms which permit scientists to genetically distinguish one individual from another. (Dimond Declaration, ¶ 9).

The particular genetic information or base sequence associated with a segment of DNA at a particular STR locus in one individual, is called an "allele." (Dimond Declaration, ¶ 10). As noted in the '598 Patent, an "allele" is "a genetic variation

[7] Although use of one locus is insufficient to positively "match" a DNA sample to an individual, differences in the DNA sequence between a DNA sample and an individual's DNA are sufficient to conclusively prove exclusion, *i.e.*, that the DNA sample of interest is not from the human subject.

associated with a segment of DNA, *i.e.*, one of two or more ***alternate*** forms of a DNA sequence occupying the same locus." (Emphasis added). The alleles are numbered in accordance with the number of repeated nucleotide motifs (the "motif" is the specific nucleotide sequence, e.g., AATG, of the short tandem repeat). (*Id.*)

B. Overview of the Promega Patent Method Claims

The Promega Patents have numbered claims which specify methods or kits. The independent method claims of all four (4) Promega Patents identify very similar method steps. Those steps typically involve (a) obtaining the DNA sample(s), (b) selecting "a set of . . .[STR] loci" to be used, (c) "co-amplifying" the alleles of the selected loci and (d) evaluating the amplified alleles to determine which alleles are present. (*See, e.g.*, Claims 1, 12 and 28 of the '598 Patent; *see also* Claim 16 of the '660 Patent and Claims 1 and 13 of the '235 Patent). None of the independent method claims of the Promega Patents mention the term "primer." Importantly, these method steps of the independent method claims of the Promega Patents all follow a preamble for each independent claim which ends with the open-ended term "comprising."

To understand the meaning of "a set of . . . loci" in step (b) of these claims, one can go directly to definitions in the specifications. For example, as noted in the '598 Patent (Col. 5, lines 30-31) a "locus" is a "specific position on a chromosome." The language of the independent claims themselves indicates the "set of loci" are being "selected . . . to be analyzed." The sets of specified loci are illustrated in the body of the claim – but step b) of Claim 1 of the '598 Patent indicates one is to select "at least" three loci. Thus, it is clear that one of the specified sets of three loci must be selected but additional loci could also be included in the set. Step b) of Claims 12 and 28 indicates the set "comprises" the three loci (indicating that the set is open-ended). Likewise, step (b)

of independent Claims 1 and 13 of the '235 Patent specifies comprising, indicating that the set can have more than the 13 loci identified in those claims.

To understand the meaning of the term "co-amplifying" in step (c) of these various independent method Claims of the Promega Patents, it is helpful to consider the commonly known scientific term "amplifying." The term "amplify" refers to a process in which multiple copies of the alleles present at the STR loci are made. (Dimond Declaration, ¶ 11). The STR regions of the DNA must be "amplified" to be visualized or detected because they are present in too low a concentration to be detected among the rest of the human DNA. (Dimond Declaration, ¶ 11). The Polymerase Chain Reaction (PCR) is illustrative.

PCR is "a technique in which cycles of denaturation, annealing with primer, and extension with DNA polymerase are used to amplify the number of copies of a target DNA sequence . . ." ('598, Col. 5, lines 38-41). First, the "double stranded" or two strands of genomic DNA are separated or "denatured," thereby forming "single stranded" DNA. This denaturation step is done by heating the DNA to a certain temperature, which is sufficient to cause the two strands to separate. (Dimond Declaration, ¶ 12). Second, a pair of PCR "primers" is introduced and allowed to hybridize or pair with the single stranded DNA. (*Id.*)

"Primers," are described in the Promega Patent specifications as "two single-stranded oligonucleotides . . . which hybridize with opposing strands of a locus . . ." ('598 Patent at Col. 5, lines 57-58).[8] "Hybridization" occurs when the PCR primers "anneal" or join to a single strand of the DNA. This hybridization occurs in accordance

[8] It should be noted that there is a definition of "primers" or "primer" in the specifications of all of the Promega Patents and these definitions are consistent with how the term is understood to one skilled in the art. (Dimond Declaration, ¶ 13). The term is not defined with respect to specific sequences.

with the nucleotide pairing rules (*e.g.*, A with T, etc.) noted above at a point on the single stranded DNA where the PCR primer sequence is complementary to the genomic nucleotide sequence. (Dimond Declaration, ¶ 12). Primers are used in pairs in PCR amplification of STRs because one primer hybridizes to one of the two denatured single stranded DNA molecules at a location on the genomic sequence that precedes the STR locus and the other primer hybridizes to the other single stranded DNA molecule at a point following the STR locus:

> two primers including primer 1 that hybridizes to a single strand at one end of the DNA sequence to be amplified and primer 2 that hybridizes with the other end on the complementary strand of the DNA sequence to be amplified.

('598 Patent at Col. 5, lines 61-65). Because of this orientation, referring to the two opposing primers as the "forward" or "reverse" PCR primer differentiates each primer in the pair. (Dimond Declaration, ¶ 12). The PCR primers hybridize at a point on the genomic DNA that is adjacent to, or "flanks," the actual STR locus:

> STR loci may be amplified via the polymerase chain reaction (PCR) by employing specific primer sequences identified in the regions flanking the tandem repeat.

('598 Patent at Col. 1, lines 48-50). These "flanking regions" are used as the point of hybridization because they are not polymorphic, *i.e.*, they contain the same sequence of nucleotides for all individuals within a given population even though the number of repeats contained in the STR locus between the flanking regions varies from individual to individual. (Dimond Declaration, ¶ 14). That loci and primers other than those in the examples are intended is apparent from specification language. (*See, e.g.*, '660, Col. 12, lines 46-56; '598, Col. 6, lines 17-20).

The third step of the PCR process is extension of the primers in which each single stranded DNA molecule is made into a double stranded molecule. (Dimond Declaration, ¶ 15).An enzyme known as a "DNA polymerase" accomplishes this extension process. (*Id.*) The polymerase reads the sequence of the single stranded DNA beginning at the primer location and attaches the complementary nucleotides to the strand (As to Ts and Cs to Gs), thereby making it double stranded. (*Id.*) Finally, the first three steps are repeated many times, *i.e.*, the process is cycled, doubling the number of double-stranded fragments each time so that the number of fragments grows exponentially through this temperature cycling process. (*See* U.S. Patents Nos. 4,683,195 and 4,683,202 (which were incorporated by reference in the '598 Patent at Col. 5, lines 43-45)[9] for a discussion of the cycling and the exponential production in PCR).

The PCR process explained above describes a method for the amplification of a single STR locus. As noted earlier, the determination of the alleles present at only one STR locus will not provide meaningful statistical data for genetic identity purposes. (Dimond Declaration, ¶ 6). As a result, the amplification process must be carried out using additional STR loci. Amplifying the alleles present at a single STR locus is commonly referred to as a "monoplex" reaction. (Dimond Declaration, ¶ 16). If one wanted to use eight STR loci in an analysis of a particular sample, one could carry out eight separate monoplex reactions amplifying eight separate STR loci. (*Id.*) Monoplexing was the initial method employed when using STR loci for DNA analysis. (*Id.*) It became clear that the ability to analyze two or more loci simultaneously in a single reaction, *i.e.*, in a "multiplex" reaction, would be beneficial. As explained in the Promega Patents:

[9] Material that is incorporated by reference is to be treated as part of the specification. *See* MPEP 2163.07(b) ("The information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed").

> To minimize labor, materials and analysis time, ***it is desirable to analyze multiple loci and/or more samples simultaneously***. One approach for reaching this goal involves ***amplification of multiple loci simultaneously in a single reaction***. ***Such "multiplex" amplifications*** have been described extensively in the literature.

('598 Patent at Col. 1: 56-61). Thus, the technical definition of "multiplex" is again clear and the specification provides that generally accepted definition when it notes that this term means, "amplification of multiple loci simultaneously in a single reaction." Multiplex amplification is a process for co-amplifying loci as described in the '660 Patent, Col. 4, lines 20-22. A similar commonly accepted definition for "co-amplify" is described in the patent specifications when it notes that "co-amplify" means " . . . DNA template . . . amplified simultaneously at the individual loci . . . in a single reaction vessel" ('660 Patent at Col. 20, lines 26-28) (underlining added).

Multiplexing is key to realizing the advantages of STRs for determining genetic identity. (Dimond Declaration, ¶ 17). Often, one must be able to analyze multiple STRs from a relatively small amount of sample. That could only be accomplished if it were possible to multiplex the amplification of STR alleles in such a way that you could still determine all of the alleles present at each locus. That is what the Promega Patents accomplished. (*Id*.)

The final step, *i.e.*, step (d), in these independent method claims of Promega's Patents, is the evaluation of the amplified alleles to determine the alleles present at each locus from each DNA sample. In order to determine the amplified alleles that are present, they are typically segregated from the amplification (*e.g.*, PCR) reaction mixture or otherwise individually detected. (Dimond Declaration, ¶ 18). One such process used to

separate the alleles is known as "electrophoresis." (*Id*.) The Promega Patents acknowledge that there are a number of types of electrophoresis:

> These amplified products are generally separated by ***one of several methods of electrophoresis*** known to those skilled in the art.

('598 Patent at Col. 2, lines 7-10) (emphasis added).) In the background section of the Promega Patents, there is mention of electrophoresis using agarose gels:

> According to Fortina et al., multiplex PCR has also been used for simultaneous amplification of multiple target sequences, permitting mutant allele scanning using two lanes of an ***agarose gel***.

('598 Patent at Col. 2, lines 28-31) (emphasis added). The Promega Patents indicate that polyacrylamide gel electrophoresis (PAGE) is <u>one</u> type of electrophoresis that can be used:

> Following amplification, products are then separated by electrophoresis, *e.g.*, denaturing ***polyacrylamide gel*** electrophoresis (Sambrook et al., 1989).

('598 Patent at Col. 9, lines 30-2). The Promega Patents <u>also</u> indicate that capillary gel electrophoresis ("CE") can be used:

> Capillary electrophoresis (CE) is a molecular separation and detection system that are capable of analyzing and comparing the relative lengths of alleles of each locus amplified in a multiplex reaction.

('235 Patent at Col. 4, lines 27-29). Indeed, asserted Claim 6 of the '235 Patent encompasses both electrophoresis techniques: "wherein the amplified alleles are separated prior to evaluating in step (d), using a separation means selected from the group consisting of polyacrylamide gel electrophoresis and capillary gel electrophoresis."

While the term "gel" is used in each case, the nature of the gel need not be (and typically is not) the same for each technique. (Dimond Declaration, ¶ 19). One useful

dictionary definition (based on the Random House Dictionary) for a "gel" in the biochemistry context is found at dictionary.com:

> a semirigid polymer, as agarose, starch, cellulose acetate, or polyacrylamide, cast into slabs or cylinders for the electrophoretic separation of proteins and nucleic acids.

Agarose gels are not crosslinked and typically comprise between 1 and 3% agarose, which is a linear polymer made up of disaccharide (sugar) units. (Dimond Declaration, ¶ 19). Polyacrylamide gels used in slab gels (discussed more below) are typically crosslinked. (*Id*.) Uncrosslinked polyacrylamide is frequently used in CE, although it may or may not be called a "gel" because it may not be semi-solid. (*Id*.) The latter two systems are described below in more detail.

The polyacrylamide gel electrophoresis (or "PAGE") process typically involves the preparation of a polyacrylamide gel between two glass plates, where the gel polymerizes to form a so-called "slab gel." (Dimond Declaration, ¶ 20). The amplified alleles are then applied to a "well" at the top of the gel, and an electric current is applied to the gel. (*Id*.)

The amplified alleles will move down the lane below the well, with smaller DNA amplification products (*i.e.*, lower molecular weight products) that contain the amplified STR alleles moving down the gel faster than the larger amplification products (*i.e.*, higher molecular weight products). (Dimond Declaration, ¶ 20). The various different sizes of the amplification products are separated in this fashion and appear as "bands" on the gel. (*See, e.g.*, asserted Claim 21 of the '660 Patent: "wherein the amplified alleles are evaluated using polyacrylamide gel electrophoresis to separate the alleles, forming a polyacrylamide gel of separated alleles").

In order to actually see the DNA amplification products or bands on the gel, the DNA is stained or has labels attached to it that can be detected (see e.g., '598 Patent at Col. 2, lines 10-22). The alleles from one DNA sample can then be compared to the alleles of a second DNA sample by, for example, running the two samples side-by-side on the gel. (Dimond Declaration, ¶ 21). One can then determine whether or not the two samples came from the same individual. (*Id*.) Additionally, a "size marker" or "allelic ladder" is often run concurrently with the sample either mixed with the sample or in another lane of the gel. (*Id*.) As noted in the '598 Patent (at Col. 5, lines 16-17), an "allelic ladder" is "a standard size marker consisting of amplified alleles from the locus." By comparing the alleles amplified in the DNA sample to the allelic ladder, one can determine precisely which alleles appear in the DNA sample. (Dimond Declaration, ¶ 21).

Capillary gel electrophoresis is explained in the body of the '235 and '771 Patents. Like the PAGE technique, separation of the PCR products is based on size. (*See* '235 Patent, Col. 14, lines 62-64: "Separation of DNA fragments in a denaturing polyacrylamide gel and in capillary electrophoresis occurs based primarily on fragment size"). "Once the amplified alleles are separated, the alleles can then be visualized and analyzed" (Col. 14, lines 65 – Col. 15, line 1).

There is nothing in the specifications of the Promega Patents to suggest that the "capillary gel" must be cross-linked. (Dimond Declaration, ¶ 22). Indeed, in the examples, the polymer POP-4 is employed. (*See, e.g.*, '235 Patent at Col. 19, lines 32-33). POP-4 comprises so-called "entangled poly(N,N-dimethylacrylamide)" (or PDMA) which is not cross-linked. (Dimond Declaration, ¶ 22).

C. Overview of the Promega Patent Kit Claims

The Promega Patents also have numbered claims which specify kits. The independent kit claims identify similar components. Those components typically include "a single container containing oligonucleotide *primers for each locus* . . ." The phrase "primers for each locus" is one of the claim terms Defendants seek to construe. (*See* Exhibit A hereto; Claims 10, 23 and 33 of the '598 Patent; *see also* Claim 25 of the '660 Patent). In other kits, the primers are in "one or more containers." (*See* Claim 18 of the '235 Patent and Claim 5 of the '771 Patent). The dependent claims specify additional components such as the "allelic ladders" discussed above.

D. The Asserted Claims of the Promega Patents at Issue

In an attempt to discern the Defendants need for a construction, the Plaintiff has created a second chart which associates the asserted claims with the terms sought to be addressed. (*See* Exhibit B). As noted, some of the terms for which the Defendants seek a *Markman* ruling do not appear in any claims of a particular Promega Patent. (*See* "none" indicated on Exhibit B hereto). In some cases, a term appears in only one claim, which is typically a dependent claim. In any event, while the Defendants focus a great deal of energy on inserting specific primers into the claims, it is important to recognize that none of the asserted claims of the Promega Patents specify primers having a particular sequence.

As Exhibit B illustrates, there is very little at issue. The common bond appears to be that the terms themselves are not at issue; rather the Defendants seek to add terms not otherwise in the claims.

II. LEGAL STANDARDS

A. Claim Construction

The claims of a patent define the scope of the invention. *See Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 373 (1996). The interpretation of claim language is a question of law for the Court to decide. *Id.* at 391. In interpreting the claims, the Court should primarily look to intrinsic evidence, which includes the claim language, the specification, and the prosecution history. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-17 (Fed. Cir. 2005) (en banc). The specification "'is always highly relevant to the claim construction analysis.'" *Id.* at 1315 (quoting *Vitrionics Corp. v. Conceptronic, Inc.*, 90F.3d 1576, 1582 (Fed. Cir. 1996). The Federal Circuit has, however, "cautioned against reading limitations into a claim from the preferred embodiment described in the specification, even if it is the only embodiment described, absent clear disclaimer in the specification." *In re American Academy of Science Tech Center*, 367 F.3d 1359, 1369 (Fed. Cir. 2004); *see also Phillips*, 415 F.3d at 1328 ("In particular, we have expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment"). The reasons for not limiting the claims to the specification are numerous:

> If everything in the specification were required to be read into the claims, or if structural claims were to be limited to devices operated precisely as a specification-described embodiment is operated, there would be no need for claims. Nor could an applicant, regardless of the prior art, claim more broadly than that embodiment. Nor would a basis remain for the statutory necessity that an applicant conclude his specification with "claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112. It is the *claims* that measure the invention.

SRI Int'l v. Matsushita Elec. Corp. of America, 775 F.2d 1107, 1121, 227 USPQ 577, 585 (Fed. Cir. 1985) (en banc) (emphasis in original); *id*. at 1121, n. 14 (noting that merely

because "a specification describes only one embodiment does not require that each claim be limited to that one embodiment").

The doctrine of claim differentiation provides another reason for not reading limitations into the claims. This doctrine stems from "the common sense notion that different words or phrases used in separate claims are presumed to indicate that the claims have different meanings and scope." *Karlin Tech. Inc. v. Surgical Dynamics, Inc.*, 177 F.3d 968, 971-72 (Fed. Cir. 1999). The doctrine is at its strongest "where the limitation sought to be 'read into' an independent claim already appears in a dependent claim." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 910 (Fed.Cir.2004). Said another way, where the limitation already exists in a claim that depends from an independent claim, such a limitation should not be inserted into the independent claim. *See Seachange Int'l, Inc. v. C-COR Inc.*, 413 F.3d 1361, 1368-69 (Fed. Cir. 2005); *Envtl. Designs, Ltd. v. Union Oil Co. of California*, 713 F.2d 693, 699 (Fed. Cir. 1983), *cert. denied*, 464 U.S. 1043 (1984) (noting it would be "improper for courts to read into an independent claim a limitation explicitly set forth in another claim").

B. Issue Preclusion in the Context of Claim Construction

Generally speaking, issue preclusion can be held against those who were parties in the earlier proceeding. Issue preclusion is an equitable doctrine for the courts to apply. *See Evans v. Katalinic*, 445 F.3d 953, 956 (7th Cir. 2006). The party asserting issue preclusion must prove the following: (1) the issue is identical to the issue decided in the prior litigation; (2) the issue was actually litigated in the prior litigation; (3) the party against whom preclusion is sought had a full and fair opportunity to litigate the issue in the prior litigation; and (4) the determination of the issue was essential to a final judgment of the prior litigation. *See Adair v. Sherman*, 230 F.3d 890, 893 (7th Cir. 2000).

These factors come into play when determining whether a prior claim construction ruling should be given preclusive effect. Where parties were not "fully heard," a claim construction will not bind. *See RF Delaware, Inc. v. Pacific Keystone Technologies, Inc*., 326 F.3d 1255, 1261 (Fed. Cir. 2003) (issue preclusion applicable to claims construction ruling only where the parties were "fully heard"). However, where the parties are "fully heard," there can be issue preclusion. *See Dana v. E.S. Originals, Inc*., 342 F.3d 1320, 1324 (Fed. Cir. 2003) (claim construction given preclusive effect because parties were "fully heard").

Issue preclusion serves several policy interests, including improving judicial efficiency by conserving resources, providing uniformity of judgments, and preventing litigants from having a second bite at the apple. In addition, applying issue preclusion to earlier claim constructions supports the *Markman* philosophy of providing a uniform standard for patents:

> An important underpinning of the Supreme Court's ruling in *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996), which tasked trial court judges—as opposed to juries—with claim construction, was uniformity in the treatment of a given patent. 517 U.S. at 390, 116 S.Ct. at 1396. This concern would seem to provide ample reason to accord a preclusive effect to prior claim construction in all cases.

Kim v. The Earthgrains Co., No. 01 C 3895, 2005 WL 66071, *10 (N.D. Ill. Jan. 11, 2005).

III. ARGUMENT

A. Term: "a set of . . . loci"

Claim Term as Defined by Defendants	Defendants' Proposed Construction	Plaintiff's Proposed Construction
a set of . . . loci	A collection of only the loci listed in the claim	None of the asserted claims that require a multiplex of a defined set of loci exclude the presence of other STR loci in that required multiplex reaction.

By defining the claim term "a set of … loci" in their own proposed construction as a "collection of … loci" the Defendants appear to concede that there is no dispute as to the plain meaning of this term. What is really in dispute in this matter is: Should additional language be imported into the claims that excludes the presence of STR loci other than those specifically named in the various claims in which the term "a set of… loci" appears? The answer is no.

This Court addressed this very issue in an earlier case. (*Promega Corp. v. Applera Corp.*, 3:01-CV-244-bbc (W.D. Wis. June 10, 2002) (Order) ("June 10, 2002 Order"). Two of the Promega Patents in this case (the '598 and the '660) were at issue in the prior case. In a January 2002 Order, this Court initially construed Claim 1 of the '660 patent to be limited such that only the loci listed in the claim were part of the multiplex amplification. Promega moved for reconsideration. In a June 10, 2002 Order, this Court determined that the earlier construction was in error and adopted the construction that Claims 1 through 5 and 16 of the '660 were not limited to the loci listed in the claims ("those claims . . . do not exclude the presence of other STR loci in the multiplex reaction . . ."") (June 10, 2002 Order, p. 10). That construction was correct and continues to control the outcome of this issue.

1. This Court's Prior Ruling is Sound

There is no basis for disturbing that June 10, 2002, ruling. The intrinsic evidence has not changed. Moreover, as this Court noted, a construction that limited the claims solely to the identified loci would create the anomalous situation of having dependent claims infringed without infringement of the independent claims. This Court's June 10, 2002 Order is explicit on this point:

> Under the court's January 2, 2002 claim construction, selection and evaluation of this precise set without including other unidentified loci in the multiplex reaction would clearly infringe claim 3. Patent law provides that because claim 3 depends from claim 1, claim 1 must also be infringed [citing Wahpeton v. Frontier, 870 F.2d 1526 (Fed. Cir. 1989)] * * * However, the January 2, 2002 claim construction can be read in such a way that claim 1 would not be infringed.

(June 10, 2002 Order, p. 6.) The Court's prior decision was sound and controls. There is no need for further construction of "a set of . . . loci."

2. None of the Asserted Claims that Require a Multiplex of a Defined Set of Loci Exclude the Presence of Other STR Loci in that Required Multiplex Reaction

The intrinsic evidence establishes that none of the asserted claims that require a multiplex of a defined set of loci exclude the presence of other STR loci in that required multiplex reaction. To understand the meaning of "a set of . . . loci," one can go directly to the claims and specifications of Promega's Patents. For example, as noted in the '598 Patent, independent claim 1 states that one is to select "at least" [not just] three loci even though 3 of the "at least 3" must be selected form a defined list of sets of three loci. Claims 12 and 28 specify selecting a set "comprising" [not consists of] three loci. Likewise, independent Claims 1 and 13 of the '235 Patent specify that the selecting a set of loci comprising [not consisting of] 13 specified loci, clearly indicates that the set can, but need not, include more loci. Indeed, Claim 4 of the '235 Patent specifies that the set

of loci "***further comprises a locus*** which can be used to identify the gender of at least one source of the DNA provided in step (a)." (Emphasis added). Clearly, this indicates that independent Claim 1 (on which Claim 4 depends) is broad enough to encompass additional loci.

Moreover, as noted earlier, the preamble of all of the independent method claims of the Promega Patents end with the term "comprising." Consequently, each clearly are open-ended in the sense that each do not exclude additional steps and/or components, *e.g.*, loci.

3. This Court's Prior Ruling is Preclusive

This Court's prior ruling on this same term ought to be given preclusive effect. All of the factors for preclusion are satisfied here. *See Adair*, 230 F.3d at 893 (four-part test: i) identical issue; ii) actually litigated; iii) the party participated; iv) a substantive decision). First, the '660 claim issue of the earlier case is identical to the claim issue here. That is to say, the earlier ruling by this Court addressed whether additional language be imported into the claims that excludes the presence of STR loci other than those specifically named in the various claims.

Second the claim term itself was litigated extensively by Promega and Applera (later ABI), both initially and in reconsideration. Given the tenacity with which the parties addressed this claim term in the earlier litigation, there is little doubt that the parties were "fully heard." *See Dana*, 342 F.3d at 1324 (claim construction given preclusive effect because parties were "fully heard").

Of course, the parties in the earlier litigation did settle, but such settlement, given the full *Markman* process this Court completed, does not change the preclusive effect of that earlier Order. *See TM Patents, L.P. v. Int'l Bus. Machines Corp.*, 72 F. Supp. 2d 370,

375-79 (S.D.N.Y. 1999), *decision supplemented sub nom. TM Patents, L.P. v. IBM Corp.*, 77 F. Supp. 2d 480 (S.D.N.Y. 1999) (issue preclusion found even where parties settled). As the *TM Patents* court noted, the only reason the claim constructions were not reviewed on appeal was the fact that the parties chose to settle—something the party elected to do and for which the party cannot complain:

> However, the only reason Judge Young's conclusions were not reviewed on appeal is that the case was settled. A party who cuts off his right to review by settling a disputed matter cannot complain that the question was never reviewed on appeal. The *Markman* rulings were not vacated as part of the settlement. They therefore remain preclusive.

TM Patents, L.P., 72 F. Supp. 2d at 378. So too here, the term was fully litigated and decided without regard to a later settlement of the infringement allegations.

Third, the party against whom preclusion is sought was a participant in the earlier litigation. As explained in the Defendants own Declarations on the arbitration questions, Applera is the predecessor of ABI; ABI merged with the Defendant Life Technologies. While the name has changed, all of what was Applera is now part of the Defendant, Life Technologies. (Declaration of Traci Libby, ¶¶ 5, 6 (Dkt. #26)). Fourth, the prior decision of this Court was certainly a substantive decision. This Court's earlier Order could not have been clearer in resolving the substantial matters surrounding construction of "a set of . . . loci" (June 10, 2002 Order). Not surprisingly, courts have indicated that such *Markman* decisions should be considered preclusive by other Courts. *See Kim*, 2005 WL 66071 at *10 ("ample reason to accord a preclusive effect to prior claim construction in all cases").

There is no need to re-litigate the term proposed by the Defendants. They have litigated it before and ought not be given a second bite of the apple (or, more accurately, a 'third' bite, given its two full sets of briefs and the two prior Orders of this Court).

B. Terms: "co-amplifying . . . loci"; "multiplex amplification . . . using primers"; "primers for co-amplifying . . . loci"; "primers for each locus"; "primers flanking the loci."

Claim Term as Defined by Defendants	Defendants' Proposed Construction	Plaintiff's Proposed Construction
Co-amplifying . . . loci	When primers are used, amplifying loci together using the **specific primer sequences** listed in the patent.	None of the asserted claims that require a multiplex of a defined set of loci exclude the use of primers other than those identified in the specification.
Multiplex amplification . . . using . . . primers	Amplifying loci together using the **specific primer sequences** listed in the patent.	See Above
Primers for co-amplifying . . . loci Primers for each locus Primers flanking the loci	The **specific primer sequences** listed in the patent for each locus.	See Above

There appears to be no dispute here concerning the definition of the actual words used in the "claim terms." Even the word "primer" is simply repeated by the Defendants in their proposed construction—there is no attempt to define that word. What appears to be in dispute in this matter is: Should additional language be imported into the claims that exclude the use of primers other than those identified in the specification? The answer is no.

1. Defendants Proposed Construction is Improper Because It Imports Claim Limitations of the Dependent Claims into the Independent Claims

None of the asserted claims of the Promega Patents on their face require the use primers of any specific nucleotide sequence. Some claims do not include the word

"primer" and other claims include only the word "primers" standing alone. Yet Defendants ask that a construction of these claims be adopted that would limit the claims to the use of only primers having the primer sequences identified in the patents.

An examination of the patent claims themselves quickly dispels the Defendants suggestion to import primers of specific sequence into the claims because to do so would require ignoring the difference between dependent and independent claims. For example, independent Claim 1 of the '598 Patent is silent regarding "primers." But Claim 3[10] of the '598 Patent (a dependent claim) limits Claim 1 to specific primers associated with co-amplifying specific loci. That situation occurs repeatedly in the '598 patent. Claims 11, 26 and 34 require the use of specific primers and depend on Claims 10, 23 and 33, respectively, each of which contain no limitation requiring the use of any specific primer. The same scenario is true of:

- independent claims Claim 16 and Claim 25 of the '660 Patent and dependent Claim 18 (which depends on Claim 17, which depends on Claim 16) and dependent Claim 26 (not asserted)
- independent Claims 1 and 18 of the '235 Patent and dependent (unasserted) Claims 5 (which depends on Claim 2, which depends on Claim 1) and 20
- independent Claim 5 of the '771 patent and dependent Claim 6

Under the doctrine of claim differentiation, it is "common sense" that independent claims cannot properly be construed to include claim limitations which appear in claims which depended from those independent claims. *Karlin Tech. Inc.*, 177 F.3d at 971-72 (The claim differentiation doctrine stems from "the common sense notion that different

[10] Claim 3 of the '598 is not asserted in this case. However, whether it or other claims are asserted does not affect their impact on claim interpretation.

words or phrases used in separate claims are presumed to indicate that the claims have different meanings and scope").

2. Defendants' Proposed Claim Construction would Create an Anomaly

Defendants' proposed construction, if accepted, would create the anomaly that one could infringe a dependent claim while not infringing the independent claim upon which it depends.

According to Defendants' proposed construction, all asserted independent claims requiring a multiplex reaction must use a set of primer pairs **consisting only of** the primer pairs identified in the specification. All primers in the co-amplification reaction must come from the patents' specifications. However, claims depending from those independent claims require only that "**at least one**" of the primer pairs used in the multiplex reaction use primer pairs identified in the specification (such as claims 3 and 11 of the '598 patent, 8, 18 and 26 of the '660 patent, 14 and 20 of the '235 patent, and 6 of the 771 patent).

As a result, if Defendants interpretation were accepted, and one multiplexed loci A, B, and C with primer pairs only two of which were identified in the specification, the independent claim would not be infringed since not all primer pairs were identified in the specification. But, though the independent claim was not infringed, the dependent claim would be infringed, since the dependent claim requires that only "at least one" primer pair be identified in the specification. This anomaly, as acknowledged and avoided in the previous *Promega v. Applera* case, precludes acceptance of the Defendants' proposed constructions.

3. The Technical Definitions Are Clear from the Specifications and the Defendants Constructions Are Inconsistent with those Definitions

Aside from the many issues the Defendants must overcome to reach even a plausible basis for acceptance of their proposed importing of new terms into the claims, the proposed constructions are plainly at odds with all the intrinsic evidence.

As noted earlier, the specifications of the patents often describe commonly accepted technical definitions for the claim terms. For example, Defendants' proposed narrowing construction for "co-amplifying . . . loci"—limiting it strictly to primers identified in the specification – is unsupportable in either the definition of "co-amplify" or "loci." The technical definition of "co-amplify" provided in the specification itself is to amplify ". . . DNA template . . . simultaneously at the individual loci . . . in a single reaction vessel." (*See, e.g.*, the '660 Patent at Col. 20, lines 26-28) (emphasis added). There is no mention of primers. So too for the term "loci" (the plural of "locus")—there is no mention of primer sequences (*See, e.g.*, the '660 Patent at Col 11, lines 50-51). Indeed, the specifications make clear that additional loci and additional primers, *i.e.*, in addition to those listed in the specification, are contemplated and encompassed within the scope of the claims (see e.g., the'660 Patent at Col. 12, lines 46-56).

In the same fashion as with "co-amplify," the Defendants propose an identical narrowing construction for "multiplex amplification . . . using . . . primers" by seeking to limit it to specified primers. But this too runs counter to the accepted technical definition of "multiplex" described in the patent specification: "amplification of multiple loci simultaneously in a single reaction." (*See* '598 Patent at Col. 1:56-60.) Again, there is no mention of a limitation to specific primers. Indeed, in explaining multiplex amplification, the specification, not surprisingly, makes no mention of a universal primer limitation.

(*See* '598 Patent at Col. 1: 56-61). There is nothing in the explanation of the term "multiplex" or "multiplex amplification" in the patent specifications that would limit the claims to specific primers.

4. Nothing in the claim language of the asserted claims limits a claim to specific primers

As already noted, the claim language of the asserted claims includes no mention of a limitation to specific primer sequences. The application of common drafting rules repeatedly demonstrates that the purported limitation offered by the Defendants was not within the contemplation of these patent claims. Several examples are illustrative (*see also* Exhibit B):

- Claim 8 of the '598 Patent, for example, has the words "using . . . primers" after the words "multiplex amplification." However, Claim 8 limits the primers only in a functional way (not a structural way) by specifying the product of the amplification "do not overlap when separated to evaluate . . ." There is nothing to suggest that this functional language limits the primers to specific sequences.

- Claim 17 of the '660 Patent contains the "using . . . primers" language after "multiplex amplification." Claim 17 only limits the primers functionally to those primers which hybridize to the flanking regions. Again, there is nothing to suggest that this functional language limits the primers to specific sequences.

- Claim 25 of the '660 Patent is a kit claim which contains "at least" language after the term "primers for co-amplifying . . . loci." By using the term "at least" it is evident that more loci and primers can be employed.

- Claim 18 of the '235 Patent is a kit claim which contains "comprising" language after the term "primers for co-amplifying . . . loci." So too, Claim 5 of the '771 Patent is a kit claim containing "comprising" language prior to the term "primers for co-amplifying . . . loci." As with the term "at least," the use of "comprising" was a conscious drafting decision to use open-ended language, and as such allowed for more loci and primers to fall within the claim.

- Claims 10, 23 and 33 of the '598 are all independent kit claims which contain "comprising" language before the term "primers for each locus."

- The independent method claims of all four (4) Promega Patents only use the term "multiplex amplification" and say nothing about primers at all, let alone specific primers. Step (c) in each of these independent method claims specify "co-amplifying . . . in a multiplex amplification reaction" and do not specify "using primers." (See, for example, Claims 1, 12 and 28 of the '598 Patent; Claim 16 of the '660 Patent, and Claims 1 and 13 of the '235 Patent.)

The face of the claims themselves simply cannot support the Defendants proposed constructions.[11]

C. Term: "Gel"

Claim Term as Defined by Defendants	Defendants' Proposed Construction	Plaintiffs' Proposed Construction
Gel	A three-dimensional cross-linked network.	"a semirigid polymer, as agarose, starch, cellulose acetate, or polyacrylamide, cast into slabs or cylinders for the electrophoretic separation of proteins and nucleic acids."

Defendants' construction for "gel," provided without explanation, attempts to limit this common general term to a particular type of gel—"A three-dimensional cross-linked network." What is in dispute is: Can the Defendants add language to a common scientific term that simply is not in the claims? The answer is no.

The words "three-dimensional" and "network" are not only non-existent in the words of the claims, those terms do not even appear in any of the Promega Patent specifications (or the Tautz patent specification for that matter). Promega believes no

[11] It may be helpful to note that the technical definition for "primer" in the '771 Patent is "a single-stranded oligonucleotide or DNA fragment which hybridizes with a DNA strand of a locus in such a manner that the 3' terminus of the primer may act as a site of polymerization using a DNA polymerase enzyme." The technical definition for "primers" is "two single-stranded oligonucleotides . . . which hybridize with opposing strands of a locus . . ." ('598 Patent at Col. 5, lines 57-58). These definitions are consistent with how the term is understood to one skilled in the art. (Dimond Declaration, ¶ 13). The terms "primer" or "primers" are simply not defined with respect to specific sequences.

particular construction is needed for "gel"—it is well understood and has its common technical meaning. For example, one useful dictionary definition (based on the Random House Dictionary) for a "gel" in the biochemistry context is found at dictionary.com:

> a semirigid polymer, as agarose, starch, cellulose acetate, or polyacrylamide, cast into slabs or cylinders for the electrophoretic separation of proteins and nucleic acids.

The nature of each of these polymers is different. Agarose gels for electrophoretic separation are typically not crosslinked, while the polyacrylamide in slab gels is typically crosslinked. (Dimond Declaration, ¶ 19). Thus, there is no scientific basis for insisting that the term "gel" be limited to crosslinked materials.

It is important to recognize that "gel" is often used in the Promega Patent specifications without reference to a specific gel type. (*See,* '598 Patent, Col.9, lines 57-61; '660 Patent Col.5, lines 29-36). Many claims do not limit the type of gel beyond the category polyacrylamide, polyacrylamide gel electrophoresis (PAGE) or capillary gel electrophoresis (CE). (*See,* '598, Claims 5, 22 & 31; '660, Claims 21 & 23; '235, Claim 6).

The '984 Tautz Patent primarily uses the term gel in its unmodified general sense throughout the specification and in the claims. For example Claim 25 is limited only to "a suitable electrophoretic gel," which would be understood to include both uncross-linked (agarose) and cross-linked gels. (Dimond Declaration, ¶ 23).[12]

In sum, there is no basis for limiting the claims in the manner Defendants suggest for the term "gel." This is particularly true here, where Defendants propose introducing

[12] As the Defendants have not specified what claims or patents are being addressed by their proposed definitions, nor explained how the definition of gel that is commonly accepted would be any different in the '984 Tautz patent, there is not much that can be said at this stage.

terms that do not even appear in the specifications.

CONCLUSION

Defendants' constructions attempt to narrow the claims—in all cases by importing language from the specification (or elsewhere). But this is an old game uniformly rejected. *White v. Dunbar*, 119 U.S. 47, 51-52 (1886) (the specification provides the context for understanding, but not for making a term "different from what it is.")

The intrinsic evidence of the Promega Patents controls, and the Defendants' proposed constructions must be rejected.

Respectfully submitted this 30th day of March, 2011.

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